11:15

786-4 Cigarette Smoking Inhibits Basal but not Stimulated Release of Nitric Oxide from the Forearm Vasculature

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To evaluate the effects of cigarette smoking on endothelial function, we examined forearm vascular responses to the intra-brachial infusion of methacholine (MC), N^G-monomethyl-L-arginine (L-NMMA) and sodium nitroprusside (SN) in 36 smokers (S) and 11 non-smoking (NS) control subjects. Values are presented as means ± standard deviation. The mean age of S (42 ± 7 years) was similar to NS (43 ± 11 years). Blood glucose, total and HDL-cholesterol and serum fibrinogen concentrations were not different between groups. S had elevated carboxyhemoglobin levels compared with NS (5.1 ± 2.5% vs, 1.1 ± 0.3%, $p < 0.001$). The incremental infusions of MC increased forearm blood flow (FBF) (ml/100 ml/min) from 3.6 ± 1.2 to 12.7 ± 8.9 in S and from 3.1 ± 0.8 to 14.7 ± 7.5 in NS (p = NS). SN increased FBF (ml/100 ml/min) from 3.7 ± 1.4 to 9.0 ± 4.7 in S and from 2.8 ± 0.3 to 8.4 ± 4.7 in NS (p = NS). L-NMMA reduced FBF (ml/100 ml/min) more ($p = 0.03$) in NS (3.9 ± 0.5 to 2.2 ± 0.7) than in S (4.1 ± 1.5 to 3.3 ± 1.2) but did not attenuate the dose response curves to MC infusion in either group.

Conclusion: Chronic cigarette smoking appears to impair basal but not stimulated release of endothelium-derived nitric oxide from the forearm vasculature.

11:30

786-5 Risk Factor Modification Improves Flow-Mediated Brachial Artery Vasoactivity but not Cold Pressor Vasoactivity in Men with Coronary Artery Disease

Mary C. Corretti, Gary D. Plotnick, Michael Miller, Robert A. Vogel. *University of Maryland Hospital, Baltimore, MD*

Coronary risk factors are associated with impaired endothelium-mediated vasoactivity in the peripheral and coronary circulation. To determine the effect of risk factor modification (RFM) on brachial artery vasoactivity, we studied 23 men with coronary artery disease (CAD). Using 7.5 MHz ultrasound, brachial artery diameter changes (%Δ Diam) in response to flow mediated (FM) and cold pressor (CP) stimuli were measured in 13 men 1 week after the initial presentation of ischemic heart disease and in another 10 men 1 year after aggressive risk factor modification, (smoking cessation, lipid lowering).

Chronically managed patients had significantly lower total cholesterol and smoking frequency.

	Acute vs.	Chronic CAD
Age (yrs):	46	46
Chol (mg/dl):	219	171*
HDL (mg/dl):	36	32
Smoking:	63%	6%*
BP (mmHg):	123/71	130/80
FM (% Δ Diam):	4.8%	10.9*
CP (% Δ Diam):	-2.4%	-2.3%

*$p < 0.01$

FM vasoactivity normalized with risk factor modification and was similar to our controls 11.5 ± 7.0%. CP response remained abnormal despite chronic RFM. This suggests that FM vasoactivity is dependent on risk factor status, but CP vasoactivity may be dependent on the presence of CAD.

11:45

786-6 Brachial Artery Vasoactivity: Cold Pressor but not Flow-Mediated Responses Correlate with the Presence of Coronary Artery Disease

Robert A. Vogel, Mary C. Corretti, Gary D. Plotnick. *University of Maryland School of Medicine, Baltimore, MD*

Flow-mediated brachial artery vasoactivity is abnormal in patients with coronary artery disease and cardiac risk factors. Cold pressor coronary artery vasoactivity is abnormal in patients with coronary disease, but brachial artery responses have not been studied. The purpose of this study was to assess whether cold pressor and flow-mediated brachial artery vasoactivity correlate independently with the presence of coronary artery disease. We studied 50 men (27 clinically normal, 23 angiographically proven coronary artery disease) ranging from 23 to 59 years old. Using 7.5 MHz ultrasound, we measured brachial artery diameter and Doppler flow velocity at baseline, during contralateral ice water hand immersion (cold pressor), following five minutes of ipsilateral blood pressure cuff occlusion (flow-mediated) and following nitroglycerin administration. During cold pressor stimulation, mean brachial artery diameter increased 0.36 ± 2.93% in the normal subjects but decreased 2.38 ± 3.32% in the coronary disease subjects ($p = 0.006$). Cold pressor vasoactivity correctly predicted the presence of coronary disease in 76% of the subjects using a predetermined criterion. Mean flow-mediated diameter increased 9.11 ± 6.01% and 6.58 ± 7.50% in the normal and coronary disease subjects, respectively (P = NS). Responses to sublingual nitroglycerin were the same in the two groups. Using multiple stepwise regression analysis, cold-pressor vasoactivity was found to be dependent upon smoking status ($p = 0.0002$) and the presence of coronary disease ($p = 0.04$). In the 32 non-smokers undergoing assessment, the presence of coronary disease was the only significant determinant of cold pressor vasoactivity ($p = 0.02$). Flow-mediated vasoactivity was found to be dependent on smoking status ($p = 0.005$) and baseline brachial artery diameter ($p = 0.02$). Flow-mediated vasoactivity correlated with total cholesterol by univariate but not multivariate analysis. The associations of brachial artery vasoactivity with cardiac risk factors and coronary disease appear to be stimulus dependent. Cold pressor vasoactivity correlates more closely with the presence of coronary disease than does flow-mediated vasoactivity. These findings suggest that abnormal cold pressor vasoactivity is a generalized vascular marker for atherosclerosis, but that flow-mediated vasoactivity correlates with the presence of risk factors.

787 New Concepts in Angiotensin Converting Enzyme Inhibition

Wednesday, March 22, 1995, 10:30 a.m.–Noon
Ernest N. Morial Convention Center, Room 26

10:30

787-1 ACE Inhibition Acutely Stimulates Sympathetic Tone and Improves Myocardial Contractility and Coronary Flow in Coronary Artery Disease. A Bradykinin-related Effect?

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The acute effects of ACE inhibition on neurohormonal activation are complex. Sympathetic tone decreases as a direct result of angiotensin II reduction; however, an increase in bradykinin may stimulate sympathetic tone. Consequently, divergent coronary and systemic hemodynamic effects may ensue. As these acute ACE inhibitor effects are incompletely identified in humans, 49 pts with significant (>70%) CAD received enalaprilat, perindoprilat or captopril intravenously, which resulted in immediate (≤5') 73% ACE inhibition and a 52% reduction in arterial angiotensin II. Twenty-two patients received placebo. During a 15-minute study protocol, placebo induced no changes. In the treated group, arterial norepinephrine (NE) increased at 5 and 15 minutes by 11% and 12%, respectively, and arterial epinephrine (E) by 11% and 14%, respectively. Heart rate did not change, but contractility (V_{MAX}) increased by 13% and 4%, respectively. Mean arterial pressure (MAP) decreased by 2% and 5% and systemic vascular resistance (SVR) decreased by 4% and 7%, respectively. Despite the reduction in coronary perfusion pressure, coronary blood flow (CBF) increased by 8% at 5 minutes, while coronary vascular resistance (CVR) decreased by 10% and 11%, respectively, at 5 and 15 minutes. Arterial 6-keto-F2α, the prostacyclin metabolite, was 52% higher compared to placebo, but increased late, at 15 minutes. Other prostaglandins and cardiac neurohormonal balances remained unaltered. Thus, in contrast to the well-known modulation of sympathetic activity by chronic converting enzyme inhibition, acute ACE inhibition results in an immediate increase in circulating catecholamines and improves myocardial contractility and coronary flow. The effect on sympathetic tone and contractility cannot be explained by changes in circulating angiotensin II and prostaglandins or cardiac renin-angiotensin, which suggests a bradykinin-related effect.

10:45

787-2 Addition of ACE Inhibitors to Beta Blockers or Calcium Channel Blockers Improves Mortality in Patients with CAD

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Patients (n = 3676) with the diagnosis (Dx) of CAD discharged from our institution from 1/88 and 1/93 were followed for a mean duration of 33.3 months. Using multiple logistic regression, with all cause mortality as the end point, combinations of therapy (Rx) with either ACE inhibitors (A) or beta blockers (B) or calcium channel blockers (C) were compared to Rx with C alone (n = 378). Age and the Dx of CHF, MI, COPD, DM, PVD, hypercholesterolemia, CABG and PTCA were entered into the model. *Results:*